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Chapter 33

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Zinc

Zinc has been known to be an essential nutrient for more than 100 years.[1] Its essentiality for plants was established early in this century,[2] and studies of its requirement for growth and in metabolism of animals soon followed.[3-5] After the recognition of zinc deficiency in swine,[6] and the description of conditioned zinc deficiency in patients with alcoholic cirrhosis of the liver,[7] zinc deficiency related to diet was characterized in adolescent boys living in the Nile Delta of Egypt[8-10] and in rural Iran.[11] In recent years, advances in technology have facilitated the study of zinc and its role in nutrition and metabolism. Zinc is now known to be involved in many biochemical processes and to have an important role in human health.

Biochemical Functions of Zinc

Zinc is essential for the function of more than 70 enzymes from different species.[12-14] In severe zinc deficiency, the activities of plasma alkaline phosphatase;[12] liver,[15] retina[16] and testicular[17] alcohol dehydrogenase; connective tissue[18] and fetal[19] thymidine kinase; pancreatic carboxypeptidase A;[12] and liver nuclear DNA-dependent RNA-polymerase[20] may be depressed.

In rapidly growing tissues, zinc deficiency usually retards the synthesis of DNA, RNA and protein and, hence, impairs cellular division, growth and repair. In intact animals, these phenomena are related to depressed utilization of amino acids[21-25] and sulfur[21,26,27] and suppressed incorporation of thymidine into DNA[19,27-30] and uridine into RNA.[31] These phenomena are probably related to a zinc requirement for activity of some of the enzymes involved. This suggestion is supported by studies in *Escherichia coli* in which DNA polymerase[32] and RNA polymerase[33] require zinc, and observations on tissue culture systems[34,35] and *Euglena gracilis*[36,37] that have shown zinc to be essential for activities of thymidine kinase, DNA polymerase, RNA polymerase and reverse transcriptase. In addition to its role in enzyme function, zinc may have a structural role in nucleoproteins that affects their function.[38-40]

Recent work suggests that zinc may have a role in the metabolism of prostaglandins or prostaglandin-mediated processes. In rats, zinc deficiency and essential fatty acid deficiency have similar effects on the animals and appear synergistic when imposed simultaneously.[41] Certain manifestations of aspirin poisoning in rats resemble those of zinc deficiency,[42] and zinc deficiency impairs aggregation of platelets exposed to adenosine diphosphate or collagen. [43]

Experimental Zinc Deficiency

In rats, severe zinc deprivation results in anorexia and cyclic feeding,[44] decreased efficiency of food utilization and impaired growth.[45] Severe dermatitis, depressed gonadal function and impaired immunity are characteristics of the deficiency in several species.[46-56] In rats, deficiency prior to fertilization and early in pregnancy impairs pre-implantation development of the embryo[57] and causes a high rate of fetal resorption and a high incidence of fetal malformations.[58] Severe zinc deficiency throughout parturition in rats prolongs labor, causes hemorrhage, and maternal death.[50,59,60] Sequelae of intrauterine zinc deficiency during the last trimester of pregnancy in rats[61] and in monkeys[54] include signs of impaired behavioral development, such as poor active avoidance of shock[62] and increased aggression[63] in rats, and decreased activity and play and poor problem-solving in monkeys.[54,64]

When nursing rat dams are fed a zinc-deficient diet, the zinc content of the milk decreases and growth of pups is retarded.[27,65] Depressed incorporation of thymidine into brain DNA,[27] impaired synthesis of brain histone proteins[24] and abnormalities in brain composition,[27,66] cellular division and maturation[67] occur in pups nursed by zinc-deficient dams. Sequelae in nutritionally rehabilitated offspring include poor maze acquisition[68] and suppressed long-[69]and short-term[70] memory.

The requirement of zinc for healing was shown by studies in animals. In response to an increased local requirement, zinc accumulates in healing tissues[71] where it contributes to the replication of fibroblasts, the synthesis of collagen, and possibly, to the cross-linking of collagen.[72-74] In zinc-deficient animals, these processes are severely impaired. Wounds close slowly and suture lines rupture relatively easily.[75,76]

Studies in animals also have established the essentiality of zinc for immune processes. Calves with lethal trait A-46, a hereditary inability to absorb zinc, exhibit thymic hypoplasia and infections which are prevented by zinc supplementation.[46] In zinc-deficient mice and rats, both humoral and cell-mediated immune functions are suppressed.[51-53,77-81]

Other effects of zinc deficiency in animals that are relevant to human nutrition are its effects on appetite control, taste acuity and brain norepinephrine levels. Rats fed diets rich in protein but deficient in zinc display cyclic feeding and anorexia.[44,82] The feeding cycle is related to the level of zinc in plasma but does not appear to relate to plasma or brain levels of tyrosine or tryptophan. Therefore, zinc nutriture, per se, appears to influence appetite. Perhaps related to effects on appetite are the abnormal taste preferences that occur in zinc-deficient rats.[83] Of uncertain significance is the increased brain norepinephrine that occurs.[84] Because concentrations of brain tyrosine increase marginally in zinc deficiency,[82] it is unclear if the increased norepinephrine is caused by increased precursor or by an alteration in enzyme activity.

Zinc Metabolism

Studies of intestinal zinc absorption in rats have yielded conflicting results. The discrepancy is probably because of differences in the techniques employed. In some studies, the duodenum has been the site of maximal absorption;[85-88] in others, maximum uptake has occurred in the jejunum and ileum.[89-92] In one study, no regional differences were detected.[93] Absorption is an active process requiring aerobic conditions.[90,94] Over a range of zinc intakes, homeostatic adaptation occurs regulating the amounts of zinc absorbed.[95] A portion of absorbed zinc is rapidly transported through the mucosal cells and a second fraction is retained in the mucosa and is released slowly over a period of hours. Kinetic analysis suggests that saturable binding sites are involved.[88] Certain hormones appear to influence zinc absorption. Reported facilitators include cholecalciferol,[90] leukocyte endogenous mediator[96] and prostaglandin E_2.[94] Metallothionine within the mucosal cell seems to have a role in controlling the amount of zinc available for movement into the circulation.[97,98] Entry into the portal circulation is thought to occur by binding to albumin.[98]

Within the intestinal lumen, a variety of factors appears to influence the availability of zinc for absorption. These factors include endogenously produced and ingested substances. Low molecular weight species such as methionine, histidine, cysteine, reduced glutathione, citrate, picolinate, prostaglandin E_2 and other small ligands have been shown to facilitate the intestinal uptake of zinc experimental systems.[97,98] The physiologic importance of some of them has been the subject of intensive research. Particular debate has centered around prostaglandin E_2, picolinic acid and citrate. The studies that suggest prostaglandin E_2 has a role in intestinal uptake of zinc seem straightforward.[94] The mechanism of the phenomenon remains to be explained. The data supporting roles for picolinic acid and citrate in zinc homeostasis are more complex. With regard to picolinate, published observations on persons with the genetic disease acrodermatitis enteropathica suggested that such patients have a defect in tryptophan metabolism proximal to the synthesis of picolinic acid.[99] The stability constant of picolinic acid with zinc ($\log B_2 = 10.01$),[100] the identification of picolinic acid in human milk and much smaller amounts in cow's milk,[101] the finding that ligation of the pancreatic duct will impair zinc absorption,[102] the presence of picolinic acid in Viocase (a pancreatic enzyme extract)[103] and the therapeutic response of infants with acrodermatitis enteropathica to supplements of zinc picolinate[103-105] are consistent with the theory. Experimental observations in rats showing that the inhibition of zinc absorption and/or retention caused by pyridoxine or tryptophan deprivation was reversed by picolinic acid,[106,107] provide physiological evidence consistent with the hypothesis that picolinic acid has a physiologic role in zinc homeostasis.[108] This hypothesis has been strongly disputed by others,[109] who have confirmed the presence of substantial amounts of citrate in milk and have demonstrated its binding of zinc.[110,111] They hypothesize that one of the functions of citrate in milk is to act as a facilitator of zinc absorption and note that citrate will facilitate zinc absorption in experimental animals.[112] They dismiss the possibility that picolinic acid may act similarly because they found much smaller amounts in human milk than had been previously reported.[113] In addition, their studies did not suggest the presence of picolinic acid in pancreatic secretions.[113] They dismiss the above cited observations on experimental animals as irrelevant.[113] Resolutions of these disagreements will depend on the results of future research. In this regard, the finding that men with pancreatic insufficiency display substantially better absorption of zinc when given zinc dipicolinate than when given zinc sulfate is of interest. Control subjects did not show better zinc absorption when given zinc dipicolinate.[114] Other evidence, although indirect, that picolinate might have a role in zinc metabolism is the finding that activity of liver and kidney picolinic carboxylase activity of lactating or tryptophan-deprived rats is increased substantially. Perhaps the increase in association with lactation represents a feedback response.[115]

Inorganic inhibitors of zinc absorption include cadmium, copper, calcium and ferrous iron.[101,112,116] In humans, the inhibitory effect of ferrous iron on zinc absorption was significant when pharmacologic amounts were administered.[117] The mechanism of inhibition by these cations is unknown. Possibilities include competition for facilitating binding ligands, receptor sites in intestinal mucosal cells or intracellular-binding ligands.

Organic inhibitors of zinc absorption include myoinositol hexaphosphate (phytate)[118,119] and components of dietary fiber,[120-123] including hemicellulose and lignin.[122,123] The inhibition of zinc absorption by phytate appears to be through co-precipitation with calcium and phytate to form an insoluble complex.[119] It seems likely that products of the Maillard reaction[124] and amino acid-phytate compounds[125] formed during food processing or cooking can also inhibit zinc absorption. Clay[126] and possibly other substances consumed by persons who practice pica may inhibit the availability of zinc for intestinal absorption. Clay eating is believed to be one of the factors contributing to the occurrence of zinc-responsive dwarfism in Iranian village children.[11,126]

The primary route of zinc excretion is via the gastrointestinal tract. When men were fed mixed Western diets while living in a metabolic ward, the level of fecal zinc was highly related to the level of dietary zinc ($n = 161$, $r^2 = 0.77$, $p < 0.0001$). Endogenous zinc enters the intestinal lumen as a constituent of metalloproteins secreted by the salivary glands, intestinal mucosa, pancreas[127] and liver, from the catabolism of intestinal cells that are sloughed into the lumen and by active transport across the intestinal mucosa.[90,95,128] Studies in rats suggest that control of zinc secretion by the intestinal mucosa is influenced by prostaglandin F_2.[93]

A secondary mode of zinc excretion is the urine. Usual levels range from 300 to 600 μg per day. Zinc complexed with Maillard browning products in parenteral fluids is readily excreted.[129,130] Zinc complexed with histidine or cysteine[131,132] may be lost in the urine as may zinc complexed with albumin in patients with nephrotic syndrome.[132,133] The increased loss of zinc in urine by patients with alcoholic liver disease[132,134] or viral hepatitis[135] appears to be related to the severity of liver injury. Excretion of zinc in urine is influenced by the levels of dietary nitrogen and phosphorus. In the men noted previously, a highly significant ($r^2 = 0.16$, $p < 0.0001$) relationship was found in 161 balance studies.

Surface loss is the third mode of excretion.[136-138] Thirteen men living in a temperate environment lost 0.5 ± 0.38 mg per day ($n = 88$) exclusive of head and hand losses.[138] In regions where the environmental temperature is high, losses are believed to exceed 1 mg per day in some instances.[136]

After intestinal absorption, zinc is concentrated initially in the liver and, subsequently, distributed to the tissues. In the plasma, about two-thirds of the zinc is loosely complexed with albumin and one-third is bound to an α-2 macroglobulin.[139] A small amount is complexed with amino acids, and possibly other ligands. Zinc complexed with albumin is readily taken up by the tissues; however, the mechanism of tissue uptake has not been characterized. Uptake by liver is positively influenced by leukocyte endogenous mediator,[140] adrenocorticotrophic hormone[141] and parathyroid hormone.[142] Indirect evidence suggests that increased amino acid utilization is associated with increased tissue uptake of zinc.[140,143,144] Redistribution of zinc in the body occurs under stress,[140] during wound healing[71] and when dietary calcium is deficient or when there is increased mobilization of bone.[145] Under usual circumstances, zinc in bone is relatively unavailable to other tissues for utilization. Zinc turns over very slowly in the body; its biological half-life is 250 days.[146] With the possible exception of zinc metallothionein, a storage form of zinc has not been identified in soft tissues.[147] Thus, if dietary intake cannot satisfy the need, the redistribution of zinc in the body requires the catabolism of metalloproteins in muscle and other soft tissues to provide zinc for locations of greatest need.

Assessment of Zinc Status

Methods for assessment of zinc status are relatively insensitive.[148] Plasma zinc is the most widely used index. In persons who are severely deficient, plasma levels are usually low. In persons with mild deficiencies, plasma values are sometimes in the normal range[149-151] of 90 to 130 μg/dl. Levels of zinc in hair may or may not be decreased in deficiency.[152] In severe deficiency, hair zinc may, in fact, be increased.[153] An apparently more sensitive laboratory index of zinc nutriture is leukocyte zinc.[154] This technique apparently reflects levels of soft tissue zinc.[155,156] Indirect assessments for zinc nutriture are provided by measurements of function noted elsewhere in this chapter. In some instances, controlled therapeutic trials with zinc may be necessary to establish a diagnosis.

Human Zinc Deficiency

Zinc deficiency related to diet was first characterized in humans by Prasad and coworkers[8,9] in adolescent boys from the Nile Delta. The principal features of the deficiency were growth failure and delayed sexual maturation. After treatment with zinc, patients matured sexually and grew taller.[10] Zinc-deficient boys and girls, studied in Iran, responded similarly to treatment.[11] Similar dwarfism, related to zinc deficiency, has been reported from Turkey,[157,158] Morocco and Portugal,[126] the United States[159] and possibly China.[160] A major factor in the pathogenesis of this syndrome is the consumption of diets rich in cereals and low in sources of readily available zinc, such as animal protein. Contributing factors include parasitic infections, geophagia and chronic infectious diseases.

Comparison of estimated zinc requirements calculated factorially[161] with reported levels in diets[144,162] suggests that mild zinc deficiency may not be a rare phenomenon in the United States and other advanced industrialized countries. The zinc content of experimental diets designed to be similar to diets consumed by poor children from the southeastern United States[163] appears to be inadequate to meet the estimated requirements of many of the children, if the zinc in the diets is only 20 percent available for intestinal absorption.[164] Similarly, the zinc content of some institutional diets for children[165] and of self-selected diets of teenage and college women[166] is marginal or deficient by this standard.

Other evidence consistent with less-than-adequate zinc nutriture in children in the United States are the findings of zinc-responsive growth failure and hypogeusia associated with low levels of hair zinc in infants and children from middle-income families,[152] the association between growth failure and low hair and plasma zinc in low-income children in Denver,[167] the inverse relationship between growth and plasma zinc of inner-city children and the lower plasma zinc of inner-city children compared to suburban children from Baltimore.[168,169]

Limited data suggest that premature infants are at particular risk of zinc deficiency because of their rapid growth.[170] Requirements of newborns are also substantial.[161] Presumably, the high zinc content of colostrum[171] helps satisfy this need. Observations on premature and mature newborn infants fed human milk, or cow's milk formula, support this impression. Their negative zinc balances were probably a reflection of inadequate zinc intakes.[172,173] In addition to the level of zinc in milk or formula, the source of the milk influences zinc nutriture of infants. Zinc in human milk is more available for absorption than is zinc in cow's milk.[172,174] Infants fed human milk have higher levels of plasma zinc than do infants fed cow's milk,[174] although human and cow's milk contain similar amounts of zinc. The lower zinc availability from cow's milk can be overcome by enrichment. With enrichment, male infants fed zinc-enriched cow's milk formula displayed more growth than did the control infants.[175]

Data on zinc nutriture of teenagers is limited. The finding of low zinc content of some self-selected diets of girls from Illinois was previously noted.[166] The finding of low plasma zinc in adolescent males, associated with zinc-responsive acne vulgaris in Sweden suggests that the diet of this group was also inadequate in zinc.[176,177]

Zinc requirements are substantially increased during pregnancy.[153] Maternal plasma zinc decreases during pregnancy.[155,178,179] Low or decreasing maternal plasma zinc early in pregnancy has been associated with maternal and fetal complications at delivery[178,180] and, in one instance, with fetal malformations.[178] In another study, maternal and fetal complications at delivery were decreased by zinc supplementation of women with plasma zinc levels below a standard in early pregnancy.[181] Others did not find a relationship between complications and maternal plasma zinc levels in early or mid-pregnancy.[179] In addition, in women with normal pregnancies an inverse relationship was found between maternal plasma zinc at mid-pregnancy and fetal size.[179] In other studies, an association between fetal abnormalities of the central nervous system and abnormal zinc nutriture has been reported.[182,183] Also, zinc levels in amniotic fluid have been related to fetal growth,[184] and to resistance to intrauterine infections.[185]

Little information is available concerning the zinc status of adults and elderly persons in the United States. A review of the literature[186] suggests an increased risk of zinc deficiency in socially isolated, economically deprived or ill persons. Inappropriate selection of foods resulting in low intakes of foods rich in bioavailable zinc such as red meat contributes to the occurrence of deficiency. In some persons, poor wound healing and impaired immunity are probably related to zinc deficiency. In elderly persons who are not otherwise ill, little evidence supports the theory that losses of taste and smell acuity are related to zinc nutriture.

In the United States and other industrialized countries, the most severe instances of zinc deficiency are not due to dietary deficiency alone. Conditioning factors set the stage for the occurrence of zinc deficiency when the diet is insufficient to provide for the increased needs caused by the conditioning factor (Table I).

The most severe manifestations of human zinc deficiency occur in infants with the genetic disease acrodermatitis enteropathica.[187,188] The disease is transmitted by an autosomal recessive gene, and the symptoms usually begin after the infants have been weaned from breast milk. Manifestations include a vesiculobullous rash that usually begins around body orifices, diarrhea, failure to thrive, infections and death. Treatment of choice is the oral administration of pharmacologic doses of zinc sulfate. Although the metabolic error causing acrodermatitis enteropathica has not as yet been identified, recent findings support the hypothesis that the infants have a defect in the tryptophan metabolizing pathway proximal to the synthesis of picolinic acid.[99,216] Infants with acrodermatitis enteropathica have responded therapeutically to physiologic levels of zinc as zinc picolinate.[103,105]

Table I
Some Potential Causes of Conditioned Zinc Deficiency

Genetic or Congenital
Acrodermatitis Enteropathica[103-105,187,188]
Hemolytic Anemias
Sickle Cell Disease[189,190]
Thalessemia[191,192]
Fibrocystic Disease[193]
Gluten Enteropathy[194-197]
Down's Syndrome[198]
Malabsorption Syndromes and Inflammatory Disease of the Bowel
Crohn's Disease[178,199-202]
Jejunoileostomy[203,204]
Gastrojejunostomy[204]
Ulcerative Colitis[199]
Blind Loops and Intestinal Diverticuli[199]
Pancreatic Insufficiency[114,204]
Alcoholic-Cirrhosis of the Liver[7,132,134]
Hepatitis[135]
Chronic Renal Failure[132,205-207]
Nephrotic Syndrome[132,133]
Injury, Inflammation and Stress[140,186,208,209]
Parasitic Diseases
Hookworm[10]
Schistosomiasis[10]
Giardiasis[159]
Iatrogenic
Parenteral or Enteral Alimentation[153,201,202,210,211]
Certain Drugs[146,212,213]
Nutritional
Alcoholism[134,204]
Protein-Energy Malnutrition[214,215]
High Dietary Fiber and Phytate[117,118-123]
Pica[11,126,154,155]
Pregnancy[155,156,178-183]

Severe zinc deficiency may also occur in patients given parenteral or enteral alimentation without adequate zinc.[153,201,202,210,211] The abnormalities that occur are similar to those of infants with acrodermatitis enteropathica. In addition to the rash, the more serious manifestations include impaired immunity, poor healing and neuropsychological abnormalities.

In most other instances of conditioned zinc deficiency, manifestations are seldom as severe as those of acrodermatitis enteropathica. Exceptions occasionally do occur, however, particularly in patients with severe intestinal malabsorption,[202] or alcoholism with cirrhosis and/or pancreatic insufficiency.[204]

Less severe manifestations of conditioned zinc deficiency that are seen in growing children are growth failure and delayed sexual maturation.[189,191,192,199,200] The findings resemble those described in zinc-deficient patients with Prasad's syndrome.[8-11]

Zinc deficiency has been produced experimentally in humans. Severe deficiency with neuropsychological signs including hypogeusia was produced by giving orally large doses of histidine, which induced massive zincuria.[131] Less severe deficiency was produced in young women by feeding a formula providing less than 0.5 mg of zinc daily for 30 days. In addition to changes in biochemical indices, the women displayed non-specific signs of infections and dermatitis.[149,217] Men have been fed diets moderately deficient in zinc for long intervals. In one study, the men displayed oligospermia and a variety of biochemical abnormalities, including low testosterone, increased blood ammonia and RNAse and a decreased serum alkaline phosphatase when fed 2.7 or 3.5 mg of zinc daily for 24 to 40 weeks.[150,218] In another study, two men displayed a decrease in respiratory quotient and a fall in serum cholesterol when diets providing 3.5 and 4.0 mg of zinc daily were fed for 16 weeks.[151] In the latter three studies, decreases in plasma zinc levels were inconsistent.

Manifestations of zinc deficiency that have stirred clinical interest include dermatitis,[188,204,210,211] poor wound healing,[190,219] impaired immunity,[153,188] growth failure,[8,10,159,189,199] hypogonadism,[8,10,159,189,199] oligospermia,[194,218] impotence,[194,218] hypogeusia,[131,206,220] poor dark adaptation[220] and neuropsychological dysfunction.[131,211] All have their equivalents in experimental or farm animals.

Manifestations of zinc deficiency in experimental animals that have not been clearly characterized in humans include effects of zinc deficiency during pregnancy, and on brain development and function. Experience with other deficiencies suggests that abnormalities similar to those in animals will occur in humans if circumstances are suitable.

Zinc Requirements

Although information on the zinc content of foods is incomplete, values for some foods have been tabulated,[221] and the contribution of some foods to zinc intake estimated.[222] The best sources of zinc are meat, seafood and poultry. Refinement of cereals lowers their zinc content. Lentils, peas, beans, nuts and seeds are important sources when meat, seafood and poultry are limited. In general, foods of plant origin are less satisfactory sources of zinc because of their lower zinc content, and, as noted previously, their phytate and dietary fiber content.

Studies in young children suggest that intakes of 7 to 8 mg of readily available zinc are adequate for growth.[137] These estimates are consistent with factorial estimates of zinc requirements.[161] Zinc requirements of children increase in the adolescent growth spurt.[164] Requirements then decrease as growth slows.

Studies of adult men living in a metabolic unit noted previously suggest that dietary zinc requirements are, in part, related to the level of dietary phosphorus and nitrogen.[144] When data from 157 28- to 30-day balance studies were evaluated by multiple stepwise regression to determine predictors of the requirement when balance is in equilibrium (Table II), dietary phosphorus was the first predictor (that is, most important predictor) selected. Dietary nitrogen was the second predictor, followed by the interaction between dietary nitrogen and phosphorus.

Eighty-three percent of the variance in requirement was explained ($p < 0.0001$). The requirement for zinc calculated from the formula (footnote to Table II) is lowest when dietary phosphorus and protein are low and highest when dietary phosphorus and protein are high. When protein is high and phosphorus is low, the requirement is nearly double the level when both predictors are low. Requirement is substantial when phosphate is high and protein is low. The practical implications of these interactions are illustrated by estimates of the zinc requirements of elderly persons who participated in the U.S. Department of Agriculture Home Food Consumption Survey. For example, in men aged 65 to 74 years whose mean protein intake was 81 g per day and mean phosphorus intake was 1.25 g per day, the mean zinc requirement was 10.1 mg per day. Zinc requirements of women were 6.5 mg per day because their intakes of protein and phosphorus were lower.[186] Greger and

Table II

Zinc Requirements (mg/day) of Men in Relation to Dietary Phosphorus and Protein[+]

	Zinc (mg)			
Protein (g)	40	60	80	100
Phosphorus (mg)				
1000	5.27	6.91	8.54	10.17
	(2.48-8.07)*	(4.11-9.70)	(5.74-11.33)	(7.38-12.96)
1500	9.11	10.27	11.42	12.57
	(6.32-11.91)	(7.47-13.06)	(8.62-14.21)	(9.78-15.36)
2000	12.95	13.63	14.30	14.97
	(10.16-15.75)	(10.83-16.42)	(11.50-17.09)	(12.18-17.76)
2500	16.79	16.99	17.18	17.37
	(14.00-19.59)	(14.19-19.78)	(14.38-19.97)	(14.58-20.16)

[+] Requirement = -1.466 + 0.23 (Zn balance) + 5.19 (P intake) + 0.40 (N intake) -0.30 (P intake -1.389) (N intake -14.646), when balance is in equilibrium (N = 157, r^2 = 0.83, P < 0.0001).

*95 percent confidence interval

Snedeker[223] also found a relationship between zinc utilization and the intake of dietary protein and phosphorus. In their study, the level of dietary phosphorus was a critical factor. The level of dietary phosphorus influenced the amount of dietary zinc needed for equilibrium. Previous estimates of zinc requirements, based on factorial calculations,[161] were not related to intake of dietary protein and phosphorus. They did, however, allow for differences in bioavailability. The 1980 recommended dietary allowance for zinc of 15 mg daily for adults does not provide for differences in bioavailability or for other dietary characteristics.[224]

Zinc Toxicity

Toxicity from usual intakes of dietary zinc has not been reported. Pharmacological amounts of zinc, however, are not innocuous. When patients with sickle cell anemia were given about 150 mg of zinc daily, some of them developed signs of copper deficiency.[225] When young men were treated with about 160 mg of zinc daily, they displayed a substantial fall in plasma high-density lipoprotein cholesterol,[226] a type of cholesterol thought to be protective against cardiovascular disease. This finding was consistent with the hypothesis based on animal studies and epidemiologic observations that high intakes of zinc in the presence of a marginal intake of copper will adversely affect cholesterol metabolism.[227] Observations on sheep showed that high intakes of zinc during pregnancy injure the fetus.[228] This effect is presumably mediated through an interference in copper metabolism. It is unknown whether similar effects occur in humans. In view of these various adverse effects of zinc, it is probably unwise for persons to self-medicate themselves with zinc. Zinc supplementation should be administered under the guidance of a physician.

Summary

Zinc is an essential element for plants, animals and man. Zinc ions are essential for the function of more than 70 enzymes from different species which include alkaline phosphatase, carbonic anhydrase, a variety of dehydrogenases, thymidine kinase, pancreatic carboxypeptidase A and liver nuclear DNA-dependent RNA polymerase. The human body contains about 1.5 grams of zinc with liver, kidney, bone, retina, prostrate and muscle being the richest tissues. Plasma zinc is bound principally to albumin but other proteins also bind a smaller percentage of zinc.

The RDA for zinc is 3 to 5 mg in infants, 10 mg in children and 15 mg per day in adults with additional amounts recommended for pregnant and lactating women. Approximately 30 percent of ingested dietary zinc is absorbed by the gastrointestinal tract and only about 5 percent is excreted in the urine.

Zinc deficiency in man results in growth retardation, hypogonadism in males, poor appetite, mental lethargy and skin changes. Zinc deficiency interacts with Vitamin A deficiency in exacerbating night blindness. The reduction in immune competence seen in various catabolic states including protein calorie malnutrition may in fact be due to zinc deficiency. □

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